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Notice of Allowability	Application No.	Applicant(s)	
	09/394,019	KOMORIYA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 1/3/05.
2. ☒ The allowed claim(s) is/are 1-15.
3. ☒ The drawings filed on 12 April 2004 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>20050303</u> . |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date <u>6/26/03</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

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An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Tom Hunter on March 2, 2005.

Examiner's Amendments to the Specification:

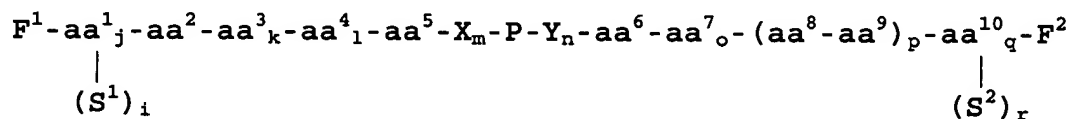
Please replace the paragraph of the specification beginning at page 1, lines 5-8 with the following paragraph:

This is a continuation-in-part of PCT/US98/0300, filed on February 20, 1998, designating the United States, which is a continuation-in-part of U.S. Application Serial No. 08/802,981, filed on February 20, 1997, now U. S. Patent No. 6,037,137, all of which are herein incorporated by reference in their entirety for all purposes.

Examiner's Amendments to the Claims:

Claims 1 and 9 have been amended as follows:

Claim 1 (Currently amended): A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein, P has the sequence Leu-Glu-His-Asp-Gly-Ile-Asn (SEQ ID NO:212);

F¹ and F² are fluorophores and F¹ is attached to the amino terminal amino acid and F² is attached to the carboxyl terminal amino acid;

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S^1 and S^2 , when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S^1 , when present, is attached to the amino terminal amino acid and S^2 , when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa^1 and aa^{10} are independently selected from the group consisting of lysine, ornithine and cysteine;

aa^2 and aa^3 are independently selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, Pro, homoserine, Aib, Thr, and Tyr;

aa^8 ; and aa^9 are independently selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa^5 , aa^4 , aa^6 , and aa^7 are independently selected from the group consisting of proline, 3,4-dehydropyrrolidine, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly, β Ala, γ Abu, Gly-Gly, Ahx, ~~C7 8-aminocaprylic acid~~, β Ala-Gly, β Ala- β Ala, γ Abu-Gly, β Ala- γ Abu, Gly-Gly-Gly, γ Abu- γ Abu, Ahx-Gly, β Ala-Gly-Gly, Ahx- β Ala, β Ala- β Ala-Gly, Gly-Gly-Gly-Gly (SEQ ID NO:223), Ahx- γ Abu, β Ala- β Ala- β Ala, γ Abu- β Ala-Gly, γ Abu- γ Abu-Gly, Ahx-Ahx, γ Abu- γ Abu- β Ala, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly, β Ala, γ Abu, Gly-Gly, Ahx, ~~C7 8-aminocaprylic acid~~, Gly- β Ala, β Ala- β Ala, Gly- γ Abu, γ Abu- β Ala, Gly-Gly-Gly, γ Abu- γ Abu, Gly-Ahx, Gly-Gly- β Ala, β Ala-Ahx, Gly- β Ala- β Ala, Gly-Gly-Gly-Gly (SEQ ID NO:223), γ Abu-Ahx, β Ala- β Ala- β Ala, Gly- β Ala- γ Abu, Gly- γ Abu- γ Abu, Ahx-Ahx, β Ala- γ Abu- γ Abu, and Gly-Ahx-Ahx;

when i is 1, S^1 is joined to aa^1 by a peptide bond through a terminal alpha amino group of aa^1 ; and when r is 1, S^2 is joined to aa^{10} by a peptide bond through a terminal alpha carboxyl group of aa^{10} .

Claim 9 (Currently amended): The composition of claim 1, wherein said fluorophore is selected from the group consisting of rhodamine X, ~~9-(2,5-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylumhalide~~ 9-(2,5-dicarboxyphenyl)-3,6-

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bis(dimethylamino)xanthylium halide or other anion, 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylium halide 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylium halide or other anion, 9-(2,5-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion (Rh6G), 9-(2,6-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion, 9-(2,5-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,6-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,5-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,6-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), carboxytetramethylrhodamine, carboxyrhodamine-X, diethylaminocoumarin, 9-(2,5-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (5-TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (6-TMR), 9-(2-carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)xanthylium, 9-(2-carboxyphenyl)-xanthylium, and a carbocyanine dye.

The following is an **Examiner's Statement of Reasons for Allowance**: The following reference appears to be the closest art to the claimed invention. Komoriya *et al.* (U.S. Patent 6,037,137) teach a fluorogenic composition for the detection of the activity of a protease having the formula cited in claim 1, where P is a peptide comprising a protease binding site for the protease, and F¹ and F² are fluorophores. The 6,037,137 patent has the same inventors as the instant application, and a terminal disclaimer has been filed. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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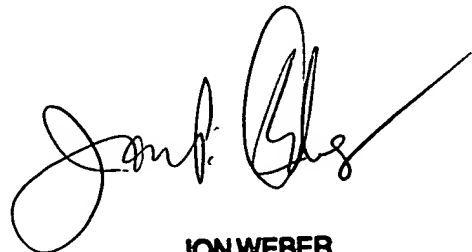
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. *CMK*

Patent Examiner

CMK

March 3, 2005

A handwritten signature in black ink, appearing to read "Jon Weber", with a large, stylized flourish extending from the end of the signature.

JON WEBER
SUPERVISORY PATENT EXAMINER